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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,969	05/08/2001	Randolph J. Noelle	037003-0280613	1327

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/849,969	NOELLE, RANDOLPH J.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/9/07, 6/20/07/ 7/10/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-10,17 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-10,17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 07/10/2007, has been entered.

As indicated previously in the Advisory Action, mailed 05/09/2007; applicant's amendment, filed 05/09/2007, has been entered.

Claim 1 has been amended.

Claims 12-14 have been canceled.
Claims 2-4, 11, 15-16, 18 and 20-21 have been canceled previously.

Claims 1, 5-10, 17 and 19 are pending and being acted upon presently as they read on anti-gp39 /anti-CD40L antibodies in the treatment of diabetes.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to request for continued examination under 37 CFR 1.114, filed 07/10/2007; Remarks presented the Pre-Appeal Brief Request for Review, filed 06/20/2007; and applicant's amended claims, filed 05/09/2007.

It is noted that the request for continued examination under 37 CFR 1.114, filed 07/10/2007, did not specifically request that the Remarks presented the Pre-Appeal Brief Request for Review, filed 06/20/2007, be considered.

The rejections of record can be found in the previous Office Actions, mailed 05/04/2006, 02/07/2007 and 05/09/2007.

Applicant's arguments, including those presented in the Pre-Appeal Brief Request for Review, and the examiner's rebuttal are essentially the same of record.

3. As indicated previously in the Advisory Action, mailed 05/09/2007; the previous rejection under 35 U.S.C. § 112, first paragraph, written description with respect to the recitation of "wherein the anti-gp39 antibody or fragment binds to an epitope recognized bound by a monoclonal antibody produced by the 24-31 hybridoma" has been withdrawn in view of applicant's amended claims, filed 05/09/2007.

4. As indicated previously in the Advisory Action, mailed 05/09/2007;
the previous rejection under 35 U.S.C. 112, first paragraph, enablement has been withdrawn in view of applicant's canceled claims 12-14.

5. Claims 1, 5-10, 17 and 19 stand rejected under 35 U.S.C.§ 103(a) as being unpatentable Lederman et al. (U.S. Patent No. 6,592,868) in view of Noelle et al. (U.S. Patent No. 5,747,037) for the reasons of record.

Applicant's arguments, filed 05/09/2007, in conjunction with the 132 Clark Declaration and Exhibits, previously filed 11/0/2006, including the Remarks presented the Pre-Appeal Brief Request for Review, filed 06/20/2007; have been fully considered but are not found convincing essentially for the reasons of record.

As indicated above, it is noted that the request for continued examination under 37 CFR 1.114, filed 07/10/2007, did not specifically request that the Remarks presented the Pre-Appeal Brief Request for Review, filed 06/20/2007, be considered.

However, given that the Remarks presented the Pre-Appeal Brief Request for Review were essentially a reiteration of applicant's arguments previously filed 11/0/2006,
applicant's argument and the examiner's rebuttal are essentially the same of record.

Therefore, the following of record is essentially reiterated for applicant's convenience.

Again, applicant has argued in conjunction with the 132 Clark Declaration / Exhibits that the prior art is based upon incorrect assumptions and that methods of inhibiting T cell-mediated immune responses at the time the invention was made with gp39 antagonists lacked a reasonable expectation of success (e.g., June 1995).

Applicant also submits that the prior art, particularly Lederman et al. is limited to inhibiting humoral or B-cell mediated immune responses and that there is no functional data in Lederman assessing the role of anti-CD40L antibody in vivo which would be essential to know if the antibody could inhibit autoimmune disease.

Applicant did acknowledge that the prior art inhibited T cell – B cell interactions and that antigen-presenting cells are important in generating immune responses.

However, it appears that applicant did not mention
that B cells are important antigen-presenting cells in humans (e.g., see Noelle et al., column 10, paragraph 1);
that Noelle et al. does teach inducing T cell tolerance or non-responsiveness via gp39 antagonists;
that both Lederman et al. and Noelle et al. (co-inventor) do teach treating autoimmunity as well as other conditions associated with T cell immune responses with gp39 / CD40L / 5C8 antagonists and
that Lederman et al. teach and claim methods of treating diabetes (e.g., see Claim 7 of Lederman et al.).

Applicant's arguments, including the reliance upon the 132 Clark Declaration and Exhibits focus on mechanisms and not on the teachings of the prior art set forth in the rejection of record.

Applicant submits that it is more than a difference in mechanism of action that distinguishes the present invention over the teachings of the prior art. The treatment of "tissue damage [that] results from a T cell mediated immune reaction to an autoantigen" by a patient with type I diabetes that is called for in the present claims is different than treating tissue damage resulting from B cell mediated immune reactions. The former involves treating inflammation and destruction of beta cells by macrophages and cytotoxic T cells, while the latter involves autoantibodies. As explained by Dr. Clark, tissue damage caused by a T cell mediated immune reaction to an autoantigen was not considered treatable by gp39 antagonists in June of 1995 (e.g., see Declaration of Clark, paragraphs 14 and 16).

Applicant submits that the evidence submitted with the 04/01/2005 Reply (Noelle Declaration (Exhibit D) and Exhibits B and C) as to the unexpected superior results of the 24-31 antibody in vivo as compared to the 5c8 antibody has not been accorded its due weight. In addition to being therapeutically safe by not causing thomboses (contrary to hu5c8), the antibodies called for in the present claims block binding of CD40 to gp39 in vivo more effectively than 5c8. This powerful objective evidence of superior results weighs heavily in favor of patentability but has been accorded little or no consideration.

In contrast to applicant's assertions,
the prior art of record is not required to provide actual efficacy for the specifically claimed methods to render the instant claims obvious.

Again, other than relying on asserted differences in mechanisms of action based upon the asserted teachings of the prior art set forth in the rejection of record and that relied upon in the 132 Declaration and Exhibits,
applicant has not distinguished between the motivation and expectation of success in treating the same patient populations, namely patients with diabetes, with the same gp39 / CD40L / 5C8 antagonists, namely gp39- / CD40L- / 5c8- specific antibodies.

Further, applicant ignores the claims of Lederman et al. (U.S. Patent No. 6,592,868).

Applicant is reminded that U.S. patents are presumed valid by U.S. courts unless proven otherwise. See 35 U.S.C. 282

While applicant and the 132 Clark Declaration are essentially indicating the treating the T cell-mediated tissue destruction associated with type I diabetes would not have been expected at the time the invention was made and that Lederman et al. does not provide any in vitro or in vivo data to support their patent,
applicant has not addressed the presumption of validity as well as the clear teachings of the Lederman et al. patent, which includes methods of treating diabetes with gp39- / CD40L- / 5C8-specific antibodies.

While Lederman et al. tests and directs the ordinary artisan to inhibiting T cell – B cell interactions with 5c8 (i.e., gp39 / CD40L) antagonists, including inhibiting humoral immune responses,
Lederman et al. is not is limited as asserted by applicant and the 132 Clark Declaration. As indicated previously, Lederman et al. do teach treating diseases and conditions associated with T cell mediated immune responses.

Even applicant and the 132 Clark Declaration note that most of the diseases listed by the prior art are primary B cell-mediated, thereby acknowledging that the prior art targeted diseases also including T cell-mediated immune responses as well.

While applicant asserts that the teachings of Noelle concerning the use of gp39 antagonists in the treatment of pancreatic allografts would not suggest treating the underlying disease of such treatment, namely diabetes.

Again, applicant appears to ignore or to dismiss the teachings of instant co-inventor's own prior art disclosure of treating autoimmunity with gp39-specific / CD40L-specific antibodies (e.g., see IV. Uses of the Method of the Invention on column 13) in addition to inducing antigen-specific unresponsiveness or tolerance (e.g., see Summary of the Invention and Detailed Description of the Invention).
It appears that applicant is making statements against their own interest.

Applicant's assertions of unexpected results do not overcome clear evidence of obviousness of treating patients with diabetes with anti-CD40 ligand antibodies, including the 24-31 antibody at the time the invention was made

As pointed out previously, although Lederman is silent about the prevention of a T cell mediated autoimmune response associated with type I diabetes, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

"{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. "In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

As noted previously, although the 5c8 antibody and the instant 24-31 antibody epitope specificities nor describe "T cell mediated autoimmune responses" per se, the prior art , including both Lederman et al. and Noelle et al. clearly provided for inhibiting cell-mediated inflammatory conditions, autoimmunity or diabetes at the time the invention was made with 5C8-specific / CD40L-specific antibodies.

In contrast to applicant's assertions, the prior art teaching of Lederman et al. is not limited to treating B cell immune responses only, given its teaching of inhibiting transplant rejection and autoimmune diseases such as diabetes.

Although applicant has argued that there is no suggestion in the '037 in merely administering the gp39 antagonist without antigen, Lederman et al. does teach treating diabetes with 5c8- (gp39-, CD40 ligand-) specific antibodies in the absence of antigen presenting cells.

In addition, autoimmunity by its very nature encompasses the presence of autoantigen.

'037 provides for a more efficient method for inducing long term specific nonresponsiveness to autoantigens by providing antigen presenting cells in methods to treat an autoimmune condition such as diabetes, already taught to be treated with CD40 ligand-specific antibodies in the absence of antigen presenting cells by Lederman et al.

Further, it has been noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

Given the assertions of unexpected results, the prior art already provides clear direction in providing for the particular 24-31 CD40 ligand-specific antibody in the treatment of diabetes at the time the invention was made.

In this case the teachings of both the primary and second references indicate success in treating diabetic patients with anti-CD40 ligand antibodies in the face of having to solve the same or nearly the same problem would have led one of ordinary skill in the art at the time the invention was made to combine the references to treat the same or nearly the same diabetic patient populations with antagonistic therapeutic anti-CD40 ligand antibodies to dampen the well known inflammatory problems associated with diabetic patients in the art.

The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Given the antagonistic properties of the particular 24-31 and 89-76 CD40L-specific antibodies taught by Noelle et al. ('037), the ordinary artisan would have been motivated to substitute these CD40L antagonists into the methods of treating autoimmune diseases such as diabetes, as taught by Lederman, given their inhibitory properties were consistent with the antagonistic CD40L-specific antibodies taught by the prior art. Noelle et al. ('037) and Lederman et al. all teach the advantages of anti-CD40L antibodies to inhibit immune responses by targeting the CD40L on T helper cells in therapeutic modalities of immunosuppression at the time the invention was made. Appliant's arguments that the prior art, including Lederman et al. are only limited to treating B cell immune response only is not consistent with the a reasonable interpretation of the prior art in the applicability of CD40L-specific antibodies in the treatment of various inflammatory or immune regulated conditions and disorders, including diabetes itself.

While the prior art anti-CD40L antibodies may have been tested with respect to parameters associated with B cell activation and immunoglobulin production, the prior art clearly teaches that CD40L was expressed on important activated CD4+ T cells that regulated various immune responses and that CD40L was targeted in conditions and disorders known to be cell-mediated at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to treat patients with diabetes with CD40L-specific antibodies,

incorporating CD40L-specific antibodies in therapeutic regimens with diabetic patients would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing such methods that would have resulted in "preventing T cell-mediated destruction associated with type I diabetes with prophylactically effective amounts of antagonistic CD40L-specific antibodies, including the reference anti-gp39 / anti-CD40L 24-31 antibody" at the time the invention was made.

Applicant's arguments are not found persuasive.

6. No claim allowed.

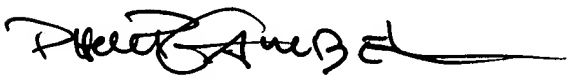
7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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